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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
SANDALS, WILLIAM O

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/058,292	Applicant(s) Hartley et al.
	Examiner William Sandals	Art Unit 1636

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less then thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 6, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *35-157* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *35-157* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Jan 30, 2002* is/are a) ☐ accepted or b) ☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Drawings

1. New formal drawings are required in this application because recent changes to the MPEP, section 608.02(c) no longer allow deferral of submission of drawings pursuant to notification. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the Patent and Trademark Office no longer prepares new drawings.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 35, 36, 40, 41, 57-59, 6-68, 7, 71, 74-77 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,159,062.

US 5,159,062 taught (see especially the summary and column 3) a method of producing a nucleic acid molecule by providing a first nucleic acid molecule comprising a first portion of a gene and a recombination site, a second nucleic acid molecule comprising a second portion of a gene and a recombination site, mixing the first and second nucleic acids with a recombination protein to recombine the first and second nucleic acids to form a third nucleic acid thereby

forming an operably linked, functional gene from the first and second portions of the gene. The gene may encode a selectable marker. The first or second portion of the gene may be fragments of the gene and may comprise a promoter. The first and second portions of the gene may be located adjacent to the gene and the first or second nucleic acid molecule may comprise a cloning site. The first, second or third nucleic acid may be an expression vector, and may be linear. The functional gene may be expressed in a host cell, and may be selected. The host cell may be *E. coli*.

4. Claims 35, 36, 40-71, 74-77 and 151-157 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 93/19172 (of record).

WO 93/19172 taught (see especially pages 19, 26-34, 46, 47, 49 and 52) a method of producing a nucleic acid molecule by providing a first nucleic acid molecule comprising a first portion of a gene and a recombination site, a second nucleic acid molecule comprising a second portion of a gene and a recombination site, mixing the first and second nucleic acids with a recombination protein to recombine the first and second nucleic acids to form a third nucleic acid thereby forming an operably linked, functional gene from the first and second portions of the gene. The gene may encode a selectable marker or a heterodimeric product. The first or second portion of the gene may be fragments of the gene and may comprise a promoter and may be PCR products. The first and second portions of the gene may be located adjacent to the gene and the first or second nucleic acid molecule may comprise a cloning site. The first, second or third

nucleic acid may be an expression vector, and may be linear. The functional gene may be expressed in a host cell, and may be selected. The host cell may be *E. coli*. The recombination sites may be loxP sites or att sites. The recombination protein may Cre, Int, IHF, Xis, FLP, gamma-delta, Tn3, Hin, Gin or Cin.

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

5. Claims 25-43, 47-50, 54-59, 68-70, 74-83, 86-89, 93-98, 102-119, 122-125, 129-134 and 138-150 are rejected under 35 U.S.C. 102(e) as being anticipated by US 5,981,177.

US 5,981,177 taught (see especially the summary and columns 9-10) a method of producing a nucleic acid molecule by providing a first nucleic acid molecule comprising a first portion of a gene and a recombination site, a second nucleic acid molecule comprising a second portion of a gene and a recombination site, mixing the first and second nucleic acids with a recombination protein to recombine the first and second nucleic acids to form a third nucleic acid

thereby forming an operably linked, functional gene from the first and second portions of the gene. The gene may encode a selectable antibiotic marker or a heterodimeric product. The first or second portion of the gene may be fragments of the gene and may comprise a promoter and may be PCR products. The first and second portions of the gene may be located adjacent to the gene and the first or second nucleic acid molecule may comprise a cloning site. The first, second or third nucleic acid may be an expression vector, and may be linear. The functional gene may be expressed in a host cell, and may be selected. The host cell may be *E. coli*. The recombination sites may be att sites.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 35-71, 74-106, 109-142 and 145-157 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,981,177 in view of WO 93/19172.

The claims are drawn to a method of producing a nucleic acid molecule by providing a first nucleic acid molecule comprising a first portion of a gene and a recombination site, a second nucleic acid molecule comprising a second portion of a gene and a recombination site, mixing the first and second nucleic acids with a recombination protein to recombine the first and second

nucleic acids to form a third nucleic acid thereby forming an operably linked, functional gene from the first and second portions of the gene. The gene may encode a selectable antibiotic marker or a heterodimeric product. The first or second portion of the gene may be fragments of the gene and may comprise a promoter and may be PCR products. The first and second portions of the gene may be located adjacent to the gene and the first or second nucleic acid molecule may comprise a cloning site. The first, second or third nucleic acid may be an expression vector, and may be linear. The functional gene may be expressed in a host cell, and may be selected. The host cell may be *E. coli*. The recombination sites may be loxP sites or att sites. The recombination protein may Cre, Int, IHF, Xis, FLP, gamma-delta, Tn3, Hin, Gin or Cin.

US 5,981,177 taught the invention as described above in the rejection under 35 USC 102 above.

US 5,981,177 did not teach that the recombination sites may be loxP sites, nor that the recombination protein may Cre, Int, IHF, Xis, FLP, gamma-delta, Tn3, Hin, Gin or Cin.

WO 93/10172 taught the invention as described in the rejection under 35 USC 102 above.

It would have been obvious to one of ordinary skill in the art at the time of filing the instant invention to combine the teachings of US 5,981,177 with WO 93/19172 because both US 5,981,177 and WO 93/19172 taught the use of a recombination protein to recombine a first and second portion of a gene to produce a functional gene by operably linking the first and second portions of the gene. The alternate use of several different recombination protein system was taught in WO 93/19172 as obvious choices to one of ordinary skill in the art.

One of ordinary skill in the art would have been motivate to combine the teachings of US 5,981,177 with WO 93/19172 because WO 93/19172 taught the obvious and well known use of alternate recombination protein systems for the desirable and beneficial use of producing a recombined, functional, operably linked gene from two portions of the gene on two separate nucleic acid segments. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of US 5,981,177 with WO 93/19172.

8. Claims 35-157 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,981,177 with WO 93/19172 as applied to claims 35-71, 74-106, 109-142 and 145-157 above, and further in view of 5,527,695.

The claims are drawn to the invention described above and also to a method of negative selection of the first or second nucleic acids in a host cell.

US 5,981,177 with WO 93/19172 taught the invention as described above.

US 5,981,177 with WO 93/19172 did not teach a method of negative selection of the first or second nucleic acids in a host cell.

US 5,527,695 taught (see especially column 7 and columns 9-10 a method of negative selection of the first or second nucleic acids in a host cell in a method of use of a recombination protein.

It would have been obvious to one of ordinary skill in the art at the time of filing the instant invention to combine the teachings of US 5,981,177 and WO 93/19172 with US 5,527,695 because US 5,527,695 taught the use of a negative selection against the cointegrates to facilitate isolation and purification of the desired recombinant gene.

One of ordinary skill in the art would have been motivated to combine the teachings of US 5,981,177 and WO 93/19172 with US 5,527,695 because US 5,527,695 taught the desirable and beneficial use of a method of negative selection against the cointegrates which facilitates the isolation and purification of the desired recombinant gene. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of US 5,981,177 and WO 93/19172 with US 5,5,27,695.

Conclusion

9. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Thursday from 8:30 AM to 7:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Zeta Adams, whose telephone number is (703) 305-3291.

William Sandals, Ph.D.

Examiner

July 14, 2002